Mechanism of Cardiac Defibrillation in Open-Chest Dogs With Unipolar DC-Coupled Simultaneous Activation and Shock Potential Recordings

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The automatic implantable cardioverter-defibrillator has been shown to dramatically improve survival. The future refinement of these devices requires a clear understanding of their mechanism of action. We performed the following study to test two hypotheses: 1) When defibrillation is successful, fibrillating activity must be annihilated in a critical mass of both ventricles; and 2) when defibrillation is unsuccessful, at least one area of the ventricular mass has been left fibrillating. Unipolar Ag/AgCl sintered electrodes were directly coupled from triangular arrays at 40 epicardial locations (total, 120 recording sites) that covered both right and left ventricular surfaces and were designed to measure the voltage gradient generated by the shock at each triangular array as well as the underlying myocardial electrical activity before and immediately after the shock. An algorithm was developed and tested that reliably scored whether a postshock activation was a continuation of the immediately previous fibrillating activity. This technique was applied to 203 defibrillation attempts in six open-chest dogs during electrically induced ventricular fibrillation. There were 139 successful defibrillation attempts and 64 unsuccessful attempts. Monophasic truncated exponential 10-msec defibrillation shocks (0.5–35 J) were delivered through an anodal patch on the right atrium and a cathodal patch on the left ventricular apex. In all cases of unsuccessful defibrillation, at least one ventricular site could be clearly identified that failed to be defibrillated. In cases of successful defibrillation two distinct patterns were observed: 1) complete annihilation of fibrillating activity at all sites or 2) nearly complete cessation of fibrillating activity with a single area of persistent fibrillation that subsequently self-extinguished within one to three activations. This single site in the second form of successful defibrillation was located in the region of minimum voltage gradient produced by the defibrillating waveform and was occasionally accompanied by dynamic encapsulation with refractory tissue as a result of a wavefront emanating from a region that had undergone successful defibrillation. These results support the hypothesis that a critical mass of myocardium must be affected for successful defibrillation and that unsuccessful defibrillation is always accompanied by residual fibrillating activity in at least one site. The results also demonstrate that the size of the critical mass required for successful defibrillation can be less than 100%. (Circulation 1990;82:244–260)

Coronary artery disease is the principal cause of death in many developed countries, and the majority of these deaths occur suddenly due to disturbances in rhythm leading to ventricular fibrillation (VF).¹ The only presently successful therapy for VF is electrical defibrillation. Since the first proposal by Mirowski et al of the concept of an automatic implantable defibrillator in 1970,² this device has been documented to dramatically reduce the expected mortality of patients with life-threatening arrhythmias, based on historical control groups.³–⁵ The future refinement of these devices requires a clear under-
standing of their mechanism of action in terminating malignant ventricular arrhythmias.

Three mechanisms of defibrillation have been proposed. The "total extinction" hypothesis\(^6\) proposes that all fibrillating activity must be extinguished from the ventricular myocardium for successful defibrillation to occur. The "critical mass" hypothesis\(^7\) suggests that successful defibrillation ensues when a critical amount of myocardium is rendered incapable of sustaining VF and that halting of the activation fronts associated with VF in all regions of both ventricles is not necessary for successful termination of VF. The presumed reentrant activity in the myocardium not affected is assumed to be left with a potential substrate insufficient for self-maintenance. The "upper limit of vulnerability" hypothesis\(^8\text{--}^{10}\) suggests that a defibrillation shock of more than 1 J produces an initial complete cessation of all activation fronts but that after a short latency period, new activation fronts, also attributed to the initial shock, emerge to reinitiate subsequent VF.

One of the critical determinants for the effective differentiation of these potential mechanisms is the ability to evaluate whether the first postdefibrillating shock activation is a continuation of the preshock activity or whether it arises de novo. The elucidation of the electrophysiological mechanisms underlying both successful and unsuccessful defibrillation has been hampered by amplifier saturation induced by the defibrillation shock that makes the immediate postshock interval impossible to observe with conventional metallic electrodes tied to AC-coupled amplifiers. One elegant approach to this problem has involved modification of the mapping system hardware to disconnect the filter sections of the amplifiers during the shock.\(^8\text{--}^{11}\)

In addition to observing the underlying myocardial electrical response to defibrillation, it is essential to measure the local voltage gradient produced by the shock to determine the cause of this myocardial response. The driving force for current flow in the myocardium is normally proportional to the voltage gradient imposed.\(^12\) One approach to the measurement of the defibrillation voltage gradient has involved placing many plunge electrodes through the heart wall, excising the heart, cutting it into slices, and then digitally reconstructing it.\(^11\) This approach is obviously limited to experimental animals. DC amplifiers offer several advantages in studies involving defibrillation.\(^13\) Such DC amplifiers can recover rapidly after being saturated by a shock potential, which when coupled to appropriate nonpolarizable electrodes with stable DC characteristics\(^14\) allow both the voltage gradient produced by the defibrillating shock as well as the immediate preshock and postshock activities to be readily visualized.

Whichever of the proposed mechanisms for defibrillation is correct has clinical significance. The total extinction hypothesis predicts that the voltage gradient produced by the defibrillation shock must achieve some minimal value throughout the ventricular mass. The first postshock activation in this setting could be identified as not being a continuation of the preshock VF by a pause between the last preshock activation and the first postshock activation. The duration of this pause would have to be greater than the expected interval due to the normal variation of activation intervals present during the preshock VF. The best electrode configuration would be the one that provides this minimal value of voltage gradient with the minimal shock energy. In contrast, the critical mass hypothesis implies that this minimal value of voltage gradient required for effective defibrillation must only be achieved in a fraction of the ventricular mass and that some sites could be present with a first postshock activation that was a continuation of the preshock VF. It has clearly been demonstrated that a critically timed stimulus can induce a transition into VF from a preceding, more-organized rhythm such as sinus rhythm, paced rhythm, and even ventricular tachycardia. To demonstrate de novo induction of VF from a previous rhythm of sustained VF, as implied by the upper limit of vulnerability hypothesis, would require demonstration that the first postshock activation in the region of earliest activation is not a continuation of the previously existing preshock VF. The purpose of our study was to apply a DC-coupled mapping system to measure both the epicardial voltage gradients produced by defibrillation and the underlying myocardial electrical activity to test which of the three current hypotheses for defibrillation is correct.

**Methods**

**Surgical Preparation**

Studies were done on six healthy mongrel dogs of either sex weighing 28–34 kg and anesthetized with 30 mg/kg sodium pentobarbitol administered intravenously and 2–3 mg/kg/hr given as necessary. Each dog was intubated with a cuffed endotracheal tube and ventilated with warmed, humidified room air with supplemental oxygen through a Siemens 900 ventilator with adjustment based on periodic measurements of arterial pH, Pco\(_2\), and Po\(_2\). Normal saline was continuously infused at 2 ml/kg/hr throughout the experiment via the femoral vein, and systemic blood pressure was monitored via an arterial line inserted into the femoral artery. In addition to continuous display of the systemic blood pressure, surface electrocardiographic leads I and aVF were monitored on an oscillographic monitor. Body temperature was maintained at 37° C with the warmed humidified ventilated air, and a heat lamp placed over the thorax controlled by a YSI 73A temperature controller (Yellow Springs Instruments, Yellow Springs, Ohio), with temperature sensed by a thermocouple placed in the midesophagus.

The chest was opened through a median sternotomy, and the heart was suspended in a pericardial cradle. The aortic root fat pad was dissected free, and a 4.0-mm Ag/AgCl reference electrode was sutured
to the aortic root to serve as the reference for all DC-coupled unipolar recordings. A bipolar pacing electrode was sutured to the right ventricular infundibulum for electrical induction of VF. The anodal titanium mesh defibrillation patch electrode (modified Medtronic model TX-7 [Promeon Division, Brooklyn Center, Minnesota], reduced to 4.5 cm²) was sutured to the right atrium–superior vena cava junction. The cathodal defibrillation patch electrode (Medtronic model TX-7, 15 cm²) was sutured to the left ventricular apex. A nylon mesh sock was then fitted to the ventricles, and stay sutures were placed to secure it so it would not slip down from the atrioventricular groove. The cables for the cathodal defibrillation patch and the bipolar pacing electrode were threaded out from under the sock, and the tripolar Ag/AgCl button electrodes were individually placed as uniformly as possible over the right and left ventricular epicardium, carefully avoiding the areas already covered with the defibrillation patch or the pacing electrode. A greater density of buttons was placed over areas of potential interest, such as the outflow tract of the right ventricle. After all buttons were placed, the heart was draped with a 4 × 4 in. sponge pad moistened with warmed saline. The sternum was approximated and then draped with a plastic sheet and a towel to maintain the heart in a moist and constant temperature environment. All animal procedures conformed to the guiding principles of the Canadian Council on Animal Care.

VF was induced with a train of 2-msec-wide pulses at twice-diastolic threshold at a pulse repetition rate of 50 Hz. After 10 seconds of VF, defibrillation was attempted with a 10-msec monophasic truncated exponential shock generated by a Medtronic Model 2394 external cardioverter-defibrillator using a 120-μF capacitor with digital leading edge voltage selection from 60–1,000 V. The defibrillation voltage applied to the patches and the current delivered were monitored on an oscilloscope for subsequent delivered energy calculations. Approximate defibrillation voltage thresholds were determined by decrementing the delivered shocks initially in 100-V increments until the first shock was unable to defibrillate. The smallest successful shock was considered the defibrillation threshold. This sequence was repeated three or four times, and the mean defibrillation voltage threshold determined. Randomly assigned initial shocks were then applied in 20-V increments centered around this approximate defibrillation voltage threshold to cluster the remaining defibrillation attempts around the defibrillation threshold. In some animals, 10-V increments were also possible. In an unsuccessful attempt, defibrillation was obtained within 5–30 seconds with a higher energy shock delivered through the same electrode pair. All defibrillation attempts were included for analysis, including second shocks after an unsuccessful initial attempt. A 3-minute interval was observed between fibrillation episodes.

**Figure 1.** Tripolar Ag/AgCl button electrodes used to determine the magnitude of the local voltage gradient at the button produced by a defibrillating shock as well as to observe the underlying myocardial electrical activity at the three adjacent unipolar recording sites. Actual recording sites are located at the apexes of an equilateral triangle 3.0 mm on a side. (See text for fabrication details.)

**Tripolar Ag/AgCl Button Electrodes**

Sintered Ag/AgCl cylindrical electrodes 0.8 mm in diameter were made as we have previously described and terminated in 0.13-mm (0.005-in.) silver wire. Buttons were machined from 7.9-mm (5/16-in.) diameter phenolic round rod with a groove for securing the button into the nylon mesh sock and with three holes in its central area. The holes were located at the apexes of an equilateral triangle 3.0 mm on a side into which the Ag/AgCl cylindrical electrodes were placed as shown in Figure 1. Phenolic was chosen for the button material because of its superior ability to bond to epoxy. Triangular geometry was chosen as the minimum number of sites to determine the voltage gradient in two dimensions and because this configuration ensures stable contact with all three sites on the epicardium. The silver wire connected to the Ag/AgCl electrode was epoxied in place and electrically connected to a flexible, multiple conductor–shielded cable that had a crimped stainless-steel strain relief, which was in turn bonded to the button. After all electrical connections were made and tested, the back of the button was molded in epoxy. The front side of the button, which contained the exposed Ag/AgCl electrodes, was polished smooth; then, each electrode was further machined from its original 0.8 mm diameter to 0.35 mm diameter using a 1.3-mm (3/64-in.) carbide end mill-machined with a hole in its center. The cavity around the remaining electrode element was filled with epoxy and then polished flat. The Ag/AgCl electrode dimension was reduced to minimize the measurement uncertainty involved in determining accurate voltages with an interelectrode distance of only 3.0 mm and to minimize the extent over which the electrode would perform its weighted averaging. Each button was initially tested in vitro in a 40-l bath with a one-dimensional voltage gradi-
ent produced by two square stainless-steel plates (20×20 cm) connected to a defibrillator.

At the end of each experiment, the heart was excised after potassium chloride–induced arrest with the sock and button electrodes in place. Each button was then replaced with a labeled marker, and the heart was fixed in 10% formalin.

**Mapping System**

The DC-coupled unipolar electrogram signals referenced to the aortic root were amplified, filtered (DC, 500 Hz), sampled at a 2-KHz rate, and analog-to-digital converted with 12 bits of resolution. Each of the 120 electrodes were attached to two amplifiers—one with a dynamic range of ±130 mV and the second of ±500 V. These 240 simultaneously obtained signals, together with electrocardiographic surface leads I and aVF, arterial blood pressure, and defibrillation trigger pulse, were simultaneously digitally recorded as part of a 384-channel simultaneous mapping system previously described.16 Signal substitution calibration techniques were used for both the ±130-mV and the ±500-V amplifiers.

Every electrogram was individually displayed together with its derivative and algorithm chosen activation points, with override capability available through user-friendly software. Time of activation (ACT) during VF was determined automatically with an algorithm based on choosing the maximum negative value of the dV/dt equal to or more than −0.5 V/sec within any 50-msec time interval. For example, if a peak dV/dt of −5.0 V/sec was found at a relative time of 50 msec with no dV/dt more negative from 0–50 msec and a peak dV/dt of −7.0 V/sec occurred at 70 msec (only 20 msec beyond the first supra-threshold event), then only the −7.0 V/sec would be chosen as an activation if in addition no additional dV/dt values more negative than −7.0 V/sec in the 70–120-msec window were observed. The search for activations would then continue anew at 120 msec. The minimal allowable interval of 50 msec was based on direct intracellular recordings at the onset of VF demonstrating an action potential duration of approximately 50–70 msec.17 This algorithm was first verified on a training set composed of known continuous VF and found to accurately determine that a single ACT-ACT interval was a continuation of the immediately preceding VF in 95% of cases. (See "Ventricular Fibrillation Characterization" for details.)

Voltage gradients were determined18 at each button by first obtaining the peak voltage at each of the three sites. Then, based on the assumption that the voltage gradient was uniform over the 4.5 mm² covered by the triangular array, the x and y components of the voltage gradient were calculated, and the resultant magnitude was determined. No attempt was made to orient the buttons uniformly; therefore, the directional information of the voltage gradient was lost. In addition to the magnitude of the voltage gradient at each button, the mean, standard deviation, and maximum-to-minimum epicardial ratio were determined for the entire set of button electrodes for each defibrillation attempt. These were found useful in assessing the stability and reproducibility of the multiple defibrillation attempts performed within a single animal.

All parameters of interest were displayed on geometrically realistic outlines of the epicardial surface viewed from the left anterolateral and the right posterolateral positions obtained from digitized views of photographs of the fixed heart with button electrode markers in place.

**Data Analysis**

The time interval from the last preshock ACT to the first postshock ACT was expressed as the number of SDs beyond the mean as measured from the previous 10 preshock ACT-ACT intervals. (See "Results" for the experimental justification for this approach.) A postdefibrillation activation was considered to be a continuation of the previous VF if the time interval from the last preshock activation to the first postshock activation was within 2 SDs from the prior mean ACT-ACT of VF for that site. This criterion was experimentally verified to correctly classify a continuation of VF in 95% of cases. An integer value designating this separation was termed the standard deviation separation (SDS) and was determined for each recording site for each defibrillation episode. The mean value from the three sites comprising a single button was termed the button SDS value. In addition, the activation sequences for at least the first two postdefibrillation activations were determined. Thus, 13 activations were determined for each of 120 sites for 203 defibrillation attempts for a total in excess of 300,000 activations included in this study.

Analysis of variance, Scheffe's multiple-range tests, and general linear model procedures were used to analyze the differences of grouped means.

**Results**

**In Vitro Measurement Technique Verification**

Due to the unusual nature of the parameters of interest needed to test the stated hypotheses, detailed preliminary evaluation of the amplifiers, the electrodes, and the analysis schemes were performed to ensure that no unknown artifacts would be introduced into the desired measurements. Typical unipolar electrogram signals are in the order of 20 mV peak to peak, whereas the maximum local voltage induced by a 10-J defibrillating shock is around 200 V, a four order-of-magnitude difference. This is not a minor local perturbation and can obfuscate accurate measurements unless specific measures are taken during the experimental design.

No single amplifier or analog-to-digital converter combination has the dynamic range to record both the underlying electrogram signal and the local shock potential. We used two amplifiers whose inputs were
both connected to the same electrode—one with a dynamic range of ±130 mV, which is sufficient for unipolar electrogram evaluation, and a second with a dynamic range of ±500 V, which was experimentally determined to be sufficient to record local shock potentials with leading edge voltages of as much as 1,000 V. The ability of the electrogram amplifier to withstand such a profound differential signal at its input and to recover rapidly was evaluated with the test setup shown in Figure 2A. This figure demonstrates that the low-level amplifier will recover within 2–4 msec after a saturating signal is applied, with the obvious consequence that no electrogram activity can be examined for at least 4 msec after defibrillation. Figure 2B shows the experimental technique used to demonstrate the ability of the high-level amplifier to render a faithful if somewhat distorted rendition of the defibrillation shock voltage, with the leading and trailing edges slowed down due to the 500-Hz lowpass filtering required to prevent aliasing. Initial tests documented the linearity of this filtered waveform with stable and reproducible measurements obtainable by taking a mean value over the center 1.0 msec of the pulse (three samples, 0.5 msec apart) that could then be referenced back to the true peak value by appropriate substitution calibration techniques.

After verifying that the amplifiers were capable of the intended measurements, the electrodes that would translate the myocardial voltages into electronic signals were tested. To simulate the simultaneous superimposition of a defibrillatory waveform of several hundred volts on a 20-mV oscillatory waveform, the two signals were orthogonally mixed in a saline bath with the electrodes under test located in the center of the mixed field in the bath. The low-level oscillatory waveform used to simulate the underlying myocardial electrogram activity was formed by a function generator with a triangular waveform with a period of 50 msec. If one simply connects a defibrillator to the output of a signal generator to couple the signals, the signal generator is usually destroyed. With such a test setup, the
sintered Ag/AgCl electrodes were tested for their suitability as shown in Figure 3A, which clearly demonstrates the ability to observe a continuous oscillatory waveform immediately after a saturating pulse has been applied. Also in this figure is shown the appearance of the same signal recorded in the simultaneous high-level amplifier, where the underlying oscillatory waveform is buried within the noise as expected. Defibrillation pulses up to the maximum produced by our defibrillator (1,000 V) still permitted a clear determination of the underlying low-level oscillatory waveform. To compare the results obtained using nonpolarizable electrodes with those using polarizable electrodes, pure silver electrodes were also tested as shown in Figure 3B, in which all waveforms were simultaneously obtained. The abrupt offset seen with silver electrodes was sufficient to saturate the low-level amplifiers, eliminating the ability to clearly see the underlying known continuous oscillatory activity. If a higher-input range was used to prevent saturation, then signal resolution would suffer because we are limited to 12 bits of resolution by the analog-to-digital converters. If the signal from the silver electrodes is high-pass-filtered to eliminate the exponential recovery component, then it could be possible to erroneously conclude that no signal was present after the shock. For these reasons, nonpolarizable Ag/AgCl electrodes were used in this study.

Ventricular Fibrillation Characterization

The ability to differentiate whether the first post-defibrillating shock activation is a continuation of the preshock activity or whether it represents the beginning of a new stream of events is critical in the elucidation of the mechanism of defibrillation. The ACT-ACT interval during VF is irregular, as is the morphology of the unipolar waveforms. As a consequence, simple template-matching schemes or cross-correlation determinations cannot be used to classify a single defibrillation activation waveform. We therefore chose a statistical approach to the problem, reasoning that over some time interval, the mean ACT-ACT interval along with its SD should provide a characterization at a single site that could then be used to test whether the next activation came from a similar population. Using a known continuous recording of VF, we tested what parameters were needed to state that the last activation in that recording was a continuation of the previous waveform with a 95% certainty. The time interval over which the statistics were obtained was not fixed in msec but rather was fixed in the number of ACT-ACT intervals to be included. We evaluated averaging intervals of five, 10, and 20 activations for this purpose as shown in Figure 4. The time from the second to last activation (simulating the last preshock activation) to the last activation (simulating the first postshock activation) was the interval to be tested. This interval was given an SDS value of 0 if it was more than 1 SD below the mean and less than or equal to the mean value, a value of 1 if it was less than or equal to the mean plus 1 SD but greater than the mean, and so on. We counted the number of times each of the SDS values were found in a test set formed of 50 unipolar recordings from two runs of continuous VF in three dogs for a total of 6,600 activations analyzed. The results of this analysis are shown in Table 1 and demonstrate that scoring a single activation correctly as being a continuation of VF using a 10-beat average and an SDS of less than or equal to 2 gave a correct result close to the desired 95% accuracy. In other words, 95% of the values for ACT-ACT during VF occurred within 2 SDs from the mean when a 10 or greater activation averaging window is chosen. We chose to use 10 activations because the classification was slightly tighter than for five beats and because it provides the same classification accuracy as if 20 beats were examined but requires one half the analysis time. Therefore, in this study in testing the first post-defibrillating activation, the mean and SD of the 10 preshock ACT-ACT intervals are used to calculate the SDS value for that activation. The value assigned to a button location was the mean SDS value for the three sites present on each button rounded up to the next highest integer and was termed the button SDS value.

Interestingly, a defibrillation shock may occur synchronous with an activation in a region that is unaffected by the shock, but then the first postshock activation would be assigned a high SDS value because the last preshock activation would have been masked. To address this possibility, we reasoned that three closely placed unipolar electrodes would observe similar waveform morphologies but would have slightly different activation times; therefore, the probability that the shock would mask the last preshock activation in all three would be reduced. For this reason and for the calculation of the local voltage gradient, a tripolar button electrode design was used in this study.

Reproducibility and Stability of Shock Field and Underlying Ventricular Fibrillation

Before examining the mechanisms involved in defibrillation, the reproducibility of defibrillating field generation and measurement was addressed as well as the reproducibility of VF from episode to episode. The stability and reproducibility of the defibrillator and the resulting voltage gradient field produced are demonstrated by the values in Figure 5 for a single representative dog. The mean value of the voltage gradient for each defibrillation episode averaged over all the button electrodes on the heart was found to be linearly related to the applied leading edge voltage. Furthermore, the fields were reproducible as shown for two leading edge voltage values in Figure 5, and the stability of the preparation over the 30 defibrillation episodes in this animal is documented by the stability of the maximum-to-minimum-voltage-gradient ratio, which should be independent of leading edge voltage within the ranges used.
Figure 3. Panel A: Results obtained in vitro with orthogonally mixed low- and high-level signals used to simulate simultaneous underlying myocardial extracellular electrograms and the defibrillation pulse when the recording electrodes are made of sintered Ag/AgCl. In a, the pulse from the defibrillator was set to the minimum setting, and the underlying low-level triangular waveform is readily visualized immediately after the shock. The same electrodes are simultaneously connected to a ±500-V amplifier, and its output is shown in b and documents a 13-V local difference. c demonstrates with the maximal defibrillator setting, independent of polarity, that the underlying triangular waveform is faithfully recorded. The slight increase in amplitude after the shock in c was documented to be an artifact produced by feedback modulation of the waveform generator by the shock-induced signal present on the recording electrodes and therefore not an artifact generated by either the recording electrodes or the DC amplifiers. In d is the companion high-level (±500 V) amplifier output for the higher-level shock. Panel B: Results obtained in vitro with the same experimental setup when two pairs of recording electrodes separated by 1 mm are used, with one pair composed of nonpolarizable Ag/AgCl in a and b and of polarizable Ag in c and d. The waveforms at the same defibrillating shock setting were obtained simultaneously with identical amplifiers. The triangular waveform in a is clearly visualized after the shock, but the identical defibrillating field creates a much larger offset potential in the DC-coupled Ag electrode recordings in c with the subsequent inability to visualize the known continuous electrical activity that was present. This offset seen with polarizable electrodes becomes more profound as the shock field is increased as shown in d. The voltage level adjacent to the defibrillating pulse artifact in each panel is the companion high-level amplifier-recorded voltage difference documenting the ability of metallic polarizable electrodes to provide similar high-level voltacic information as their nonpolarizable counterparts.
VF CLASSIFICATION ALGORITHM VERIFICATION

The stability of the VF induced before the multiple defibrillation trials was also examined for reproducibility as shown in Figure 6 for the same representative animal used in Figure 5. Figure 6 demonstrates that the mean ACT-ACT interval over both ventricles of the 10 activation intervals before the defibrillation shock were acceptably reproducible over the 30 trials examined. Additionally, the mean \( \frac{dV}{dt} \) value for the 10 activations before the shock averaged over both ventricles provided a remarkably reproducible value for each defibrillation attempt.

Successful Defibrillation With Immediate Complete Ventricular Fibrillation Termination

Immediate complete cessation of VF was established when the first postshock activation from all buttons demonstrated a button SDS value of 3 or more at each site. Of the 139 successful defibrillation attempts analyzed, this form of defibrillation was observed in 116 (83%). The locations of the first two postshock activations were varied for this form of successful defibrillation, with the majority located at buttons adjacent to the cathodal defibrillation patch. Figures 7 and 8 contain a typical example of this form of defibrillation for a 13-J defibrillation shock. In Figure 7 are displayed the epicardial voltage gradients generated by the defibrillation shock and the activation sequence of the first postshock activation. The button SDS values are included in the first postshock activation map and document that no sites were left fibrillating on the heart; therefore, the first postshock activation was initiated by a different

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**TABLE 1. Cumulative Percentage of Successful Scoring of a Single Activation of Ventricular Fibrillation for Prior Activation Counts of Five, Ten, and Twenty Activations**

<table>
<thead>
<tr>
<th>Prior averaging window length</th>
<th>( \leq \text{Mean} )</th>
<th>( \leq \text{Mean} + 1 \text{ SD} )</th>
<th>( \leq \text{Mean} + 2 \text{ SD} )</th>
<th>( \leq \text{Mean} + 3 \text{ SD} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 activations</td>
<td>43( \pm 6 )</td>
<td>79( \pm 4 )</td>
<td>91( \pm 5 )</td>
<td>94( \pm 3 )</td>
</tr>
<tr>
<td>10 activations</td>
<td>47( \pm 7 )</td>
<td>83( \pm 2 )</td>
<td>94( \pm 2 )</td>
<td>NS</td>
</tr>
<tr>
<td>20 activations</td>
<td>46( \pm 9 )</td>
<td>85( \pm 2 )</td>
<td>95( \pm 2 )</td>
<td>NS</td>
</tr>
</tbody>
</table>

All values are given as mean\( \pm \)SD.

*Significant at \( p<0.05 \).*
FIGURE 5. Representative data from a single animal demonstrating the linearity, reproducibility, and stability of the experimental preparation and the measurement technique. Top panel: Voltage gradients averaged over both ventricles for each defibrillation attempt as a function of the leading-edge voltage demonstrating the linear relation between the field produced and the defibrillating shock level. Leading-edge voltages of 200–500 V correspond to delivered energies of 2–13 J. Middle panel: Voltage gradients averaged over both ventricles for two different leading-edge voltages, which were randomly dispersed throughout the total of 30 attempts, with the results for the attempts examined grouped together for clarity. There were nine attempts at a 400-V leading-edge voltage and five attempts at 200 V, and the means and SDs are shown for each attempt, demonstrating their reproducibility. Bottom panel: Ratios of the maximum and the minimum epicardial voltage gradients found in each of the 30 defibrillation attempts in this animal, which document their stability.

FIGURE 6. Representative data (for the same animal as Figure 5) that demonstrates in the upper panel the relative stability of the activation intervals of the 10 preshock activations during ventricular fibrillation (VF) averaged over both ventricles from all recording sites for each of the 30 defibrillation attempts. Values are given mean ± SD. Lower panel: Similarly derived values for the \(\frac{dV}{dt}\) for these same activations.

mechanism. In this case, the first postshock activation arose from a site near the cathodal defibrillating patch. Of note in the electrogram recording from the earliest site indicated by an asterisk in Figure 7 and displayed in Figure 8 is the initiation of an electrogram with an initial QS deflection in the first postshock activation consistent with the observation that this site is near the origin of this activation wavefront. The mathematically calculated \(\frac{dV}{dt}\) is also displayed, without smoothing, and documents the relatively unambiguous appearance of points chosen for activation. Furthermore, the earliest site for the first postshock activation is clearly seen to change morphology by the second postshock activation, which indeed was mapped to a site near recording site B, which for its second postshock activation now demonstrates an initial QS wave. The unipolar recording technique thus provides additional qualitative information that is helpful in activation sequence determination in addition to clear indications of local activation.

Unsuccessful Defibrillation

A total of 64 episodes of unsuccessful defibrillation were examined. When a defibrillation attempt was
**VOLTAGE GRADIENT MAP**

Mean Global Voltage Gradient = 21.9 ± 10.5 V/cm  
Minimum Voltage Gradient = 8.7 V/cm  
Maximum Voltage Gradient = 58.5 V/cm  
Ratio of Max/Min = 6.7

**1st POST-SHOCK ACTIVATION MAP (and accompanying SDS VALUES)**

Total Epicardial Activation Time = 78.5 msec  
Mean Global SDS value = 10.5 ± 4.2  
Minimum Button SDS value = 5

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**FIGURE 7.** Successful defibrillation — total ventricular fibrillation (VF) termination type. Upper panel: Typical voltage gradient map from dog 10589 for a successful defibrillation shock, where all epicardial sites were documented to have had their preshock VF terminated. Stippled areas represent the cathodal defibrillation patch electrode. Solid circles on heart outlines represent locations of the 40 button electrodes, each with three recording sites. Upper panel: Number next to the button location is the voltage gradient value at that button (V/cm). For clarity, only the 10, 15, and 20 V/cm isovoltage gradient contour lines are drawn. Lower panel: Number next to the button location is the time (msec) of the minimum value found for that button for the first postdefibrillation activation relative to the earliest measured activation. The total epicardial activation time is the difference between the maximum and minimum times found from all 120 sites. Immediately adjacent to the activation time, surrounded by a small box, is the mean standard deviation separation (SDS) value determined for that button, calculated from the three recordings found on that button (termed the “button SDS value”). The minimum button SDS value for this defibrillation episode was 5. The site of earliest activation, 0.0 msec (192 msec relative to the last preshock activation at that site), is indicated by an asterisk, and six other sites are noted by curved arrows and labeled A–F. Isochrones are drawn in 20-msec steps. Site D occurs slightly earlier than would be expected by simple propagation from the earliest site and thus probably represents a fusion from a wavefront rapidly conducted over the Purkinje network. Site D is near the site of right ventricular breakthrough during sinus rhythm. (See Figure 8 for the electrograms found at the earliest site and the six other sites.) LV, left ventricle; RV, right ventricle. Values are given as mean ± SD.

unsuccessful, at least one site was always found in which first postshock activation was judged to be a continuation of the previous fibrillating activity based on an SDS value of 2 or less. For the cathodal defibrillating patch located on the left ventricular apex, which produced a minimum voltage gradient near the base of the heart and the right ventricular outflow tract, the residual fibrillating activity originated predominantly from these locations for defibrillation shock levels near defibrillation threshold. For leading edge voltage levels 100 or 200 V lower, the voltage gradients followed a similar distribution, but sites of continuing fibrillation were more scattered throughout the ventricles. If 2 or more different noncontiguous sites were recorded after the shock to be still fibrillating, then defibrillation was unsuccessful in 100% of the cases. As the leading edge voltage was further reduced below levels that yielded defibrillation success percentages of less than 25%, the effect was to further reduce the percent success and to observe additional sites with SDS values less than or equal to 2. An example of a representative unsuccessful defibrillation with multiple contiguous sites left fibrillating is shown in Figures 9 and 10 for a 5-J shock. In Figure 9 are the voltage gradients produced by the shock and the activation sequence of the first postshock activation. In Figure 10 are the electrograms obtained from the sites indicated in Figure 9, with the earliest site located near the right ventricular outflow tract, as well as six other selected sites. Of note is the earliest activation occurring near the minimum voltage gradient produced by the shock itself. The morphology of the earliest activation also is of the QS type,
consistent with the finding that this site is the origin for this activation wavefront. The open arrow in Figure 10 indicates the occurrence of saturation of the ±130-mV amplifier due to a signal presented by the myocardium or electrode after the defibrillation shock has terminated. This postshock overshoot was not observed in recordings performed near the cathodal patch. Such overshoots and their resultant amplifier saturation were never observed to last for more than 10 msec with the defibrillation patch configuration and the amplifier range employed, and their appearance could easily be differentiated from underlying activation as shown in Figure 10. For unsuccessful defibrillation, the average minimal voltage gradient value found in the six animals studied was $6.5 \pm 1.8$ V/cm (mean ± SD), with the largest value being 8.5 V/cm. In other words, no defibrillation attempt that produced a minimal epicardial value in excess of 8.5 V/cm was unsuccessful.

**Successful Defibrillation With Incomplete Ventricular Fibrillation Termination**

In 23 of the 139 defibrillation attempts (17%) that were successful, a single site of residual fibrillating activity could be found. These were most commonly clustered at defibrillation voltage levels near the defibrillation threshold. In contrast to unsuccessful defibrillation, however, the number of topologically distinct sites was never greater than one. If two geographically disparate sites demonstrated residual fibrillation after shock, then the shock was never found to be successful. All cases of this type of successful defibrillation with a single residual focus of fibrillating activity terminated within one to three activations. Of the 23 successful defibrillation attempts of this incomplete VF termination type, 10 of 23 (43%) terminated within one activation, 12 of 23 (52%) terminated within two activations, and one of 23 (4%) required three activations before termination. The single site of residual fibrillating activity was always located at, or one button site away from, the minimum voltage gradient produced by the shock. An example of this form of successful defibrillation is given in Figures 11 and 12 for a 5-J shock.

A second pattern of successful defibrillation with an initial residual area of fibrillating activity was

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**FIGURE 8.** Successful defibrillation—total ventricular fibrillation (VF) termination type. Electrogram recordings from sites designated in Figure 7 as the earliest (*) and six other selected sites. All unipolar electrogram recordings are shown with their algorithm-chosen 11 preshock activations and a first postshock activation designated the 12th activation. Relative activation times are listed adjacent to the first postshock activation numbered 12 on all waveforms and correspond to the values depicted at the button sites in Figure 7, lower panel. The standard deviation separation (SDS) values are as shown for the three recording sites on the button containing the earliest recorded activation. An expanded view of the $dV/dt$ for this earliest site demonstrates the clear distinction of underlying activation during either VF or after successful shock from the actual defibrillation shock itself. Values for $dV/dt$ for the last two activations before shock and the first postshock activation are given for this electrogram. The saturating signal associated with defibrillation has been clipped under software control in all plots for clarity of presentation. Time and amplitude scales as shown.
VOLTAGE GRADIENT MAP

Mean Global Voltage Gradient = 12.9 ± 6.3 V/cm
Minimum Voltage Gradient = 4.2 V/cm
Maximum Voltage Gradient = 30.6 V/cm
Ratio of Max/Min = 7.3

1st POST-SHOCK ACTIVATION MAP
(and accompanying SDS VALUES)

Total Epicardial Activation Time = 93.5 msec
Mean Global SDS value = 7.7 ± 5.9
Minimum Button SDS value = 1

FIGURE 9. Representative voltage gradient map and first postshock activation map for an unsuccessful defibrillation attempt near threshold in dog 10889. (Format similar to Figure 7.) Minimum button standard deviation separation (SDS) value of 1 documents that at least one site has been left fibrillating. This site is located near the right ventricular outflow tract, at the minimum of the voltage gradient, and is also the site of earliest postshock activation as indicated by the asterisk. Six additional sites are noted by curved arrows and labeled A–F in the lower panel. (See Figure 10 for the electrograms found at the earliest site and the six additional sites.)

rarely observed (three episodes in one dog) that slightly differed from the first in that it was seen at slightly lower leading-edge voltage levels, usually less than 300 V, and was characterized by a second activation wavefront present at approximately the same time as the wavefront initiated by the residually fibrillating myocardium. However, this second focus was initiated in an area in which VF was terminated as judged by the SDS value of more than 2. This second focus was located between the area of residual VF and the rest of the heart. It appeared that this second focus launched a wavefront both toward the remaining ventricular myocardium and toward the residual fibrillating tissue. The collision of these two activation wavefronts appeared to effectively surround the residual fibrillating tissue with a refractory envelope, and subsequently the fibrillation ceased within two or three beats, which is the same mode of extinction seen when this second activation front was not observed. The occurrence of this second wavefront was spontaneous, and there is no way to judge if the defibrillation attempt would have also been successful if this second wavefront was not present. No attempt was made to simulate the occurrence of this second potentially encapsulating waveform with an appropriately timed pacing stimulus. Just as in the first form of successful defibrillation with a single site left fibrillating, the site that was clearly a continuation of previous fibrillating activity in this second form was limited in our observations to a single site, and that site was located near the minimum voltage gradient. The average minimal voltage gradient produced during all forms of successful defibrillation for the six animals studied was 4.0±1.1 V/cm with a smallest value of 2.9 V/cm. In other words, no defibrillation shock producing a minimal voltage gradient of less than 2.9 V/cm was successful. When combined with the data found for unsuccessful defibrillation, a minimal voltage gradient between 2.9 and 8.5 V/cm could result in either a success or a failure to defibrillate.

Discussion

Higher-energy defibrillation causes more myocardial damage15; more rapidly depletes the batteries in an implanted device, necessitating more frequent generator changes; and requires larger generators. Even if a major technological breakthrough in capacitor or battery design is made to significantly reduce the device size, it would still be desirable to reduce the myocardial damage associated with higher-
energy defibrillation and to eliminate the need for a thoracotomy for patch placement.

The in vivo measurement of the myocardial voltage gradient produced by a defibrillation shock has been previously documented to be important in determining the response of the fibrillating myocardium. For defibrillation shocks at levels just below defibrillation threshold, the first site of initial postshock activation from which fibrillation resumed has previously been shown to be at a site of minimum potential gradient. Our findings agree with these previously published reports. One significant advantage of the technique presented for epicardial voltage gradient determination in this study is that the same conclusions were obtained by a technique that requires only an epicardial sock to be slipped over the heart and therefore has the potential to be applied in the human operating room at the time of automatic implantable cardioverter-defibrillator patch placement, similar to mapping techniques commonly used for the surgical therapy of malignant ventricular arrhythmias. Our preliminary studies of applying the defibrillation shock synchronized to the QRS complex in sinus rhythm have produced identical voltage gradient fields compared with the same shock delivered in ventricular fibrillation in normal dog hearts as might be expected. Actual button electrode locations would only need to be approximated intraoperatively, as is currently done for online surgical mapping. This would allow a minimal energy defibrillation shock to be applied synchronized with the QRS complex in sinus rhythm and the fields mapped, avoiding the need for multiple defibrillation tests in patients with extremely poor left ventricular function or in whom the arterial pressure returns to baseline only slowly after a fibrillation and subsequent defibrillation episode. The patch placement could then be optimized for the quantifiable parameter of field homogeneity before performing defibrillation threshold determinations. The extrapolation of the results presented in normal dog hearts to patients requiring an implantable defibrillator must be made with caution, however, because fibrillatory rates differ and geometrical alter-

**Figure 10.** Electrogram recordings during an unsuccessful defibrillation attempt from the sites designated in Figure 9 as the earliest (*) and the six other selected sites. (Format similar to Figure 8.) Note the standard deviation separation (SDS) values at the three electrodes forming the button with the earliest recorded activation all indicate that their respective first postshock activations are a continuation of the preshock fibrillating activity. An expanded view of the earliest of these three sites clearly shows the points chosen for activation in the derivative of the waveform (dV/dt). The open arrow on the expanded dV/dt waveform points to the occurrence of transient amplifier saturation for less than 5 msec that occurred after the shock and is easily differentiated from true activation when both the V(t) and dV/dt waveforms are examined.
**VOLTAGE GRADIENT MAP**

Mean Global Voltage Gradient = 14.8 ± 7.6 V/cm
Minimum Voltage Gradient = 5.1 V/cm
Maximum Voltage Gradient = 35.0 V/cm
Ratio of Max/Min = 6.8

**1st POST-SHOCK ACTIVATION MAP**
(and accompanying SDS VALUES)

Total Epicardial Activation Time = 105.0 msec
Mean Global SDS Value = 9.2 ± 6.2
Minimum Button SDS value = 1

Figure 11. Representative voltage gradient and first postshock activation maps for a successful defibrillation trial (incomplete ventricular fibrillation termination type) that initially had a site of residual fibrillating activity in dog 10689. (Format similar to Figure 7.) Note the minimum button standard deviation separation (SDS) value of 1 similar to unsuccessful defibrillation as shown in Figure 9 again located near the right ventricular outflow tract near the minimum voltage gradient produced by the defibrillation shock. The site of earliest postshock activation is indicated by an asterisk (*) and six other selected sites are designated by curved arrows and labeled A-F. (See Figure 12 for the electrograms recorded at these sites.)

A major finding of this study is that the progression from significantly subthreshold defibrillation shocks to shocks that completely terminate fibrillation with a nearly 100% success rate is a continuous one. For markedly subthreshold defibrillation shocks, multiple areas are left fibrillating, and VF resumes initiated from multiple sites. As one approaches the defibrillation threshold, greater volumes of fibrillating tissue are terminated with resultant smaller areas left fibrillating, and the locations of these residual areas lie in regions in which the voltage gradient field produced by the shock is lowest. Near threshold, if a single site is left fibrillating, it can either go on to reinitiate global VF or not, depending on factors that appear to be randomly distributed, and may be related to the geometry of the prior activation loops, fiber orientation, loading effects presented by the adjacent nonfibrillating ventricular muscle, and shock field direction. Of these four, the activation loop and loading effects are variable. The result of this heterogeneity of response at shock levels near threshold is that for identical voltage and current shocks in the same animal that produce identical voltage gradient fields, we have observed each of the three possible scenarios, namely, unsuccessful defibrillation, successful defibrillation of the complete termination type, or successful defibrillation of the partial VF termination type. The voltage gradient range over which this overlap occurs is most probably the basis for the well-documented "probability of defibrillation curve" rather than a discreet demarcation between success and failure to defibrillate. For clinical applications, techniques to ensure an operating point well within the total VF termination window would obviously be desirable.
Our conclusions are based on a direct analysis approach to the question of whether the first postshock activation is a continuation of the preshock fibrillating activity. In all unsuccessful defibrillation attempts examined in the present study using continuous DC-coupled recording techniques, at least one site was clearly found that was judged to be a continuation of the previous fibrillating activity at that site. Similarly, in no case did we find VF to be uniformly terminated and then fibrillation to be regenerated de novo. We have made every effort to verify that our algorithms for choosing activations during VF are statistically valid and that our mapping tools are free from unknown artifacts. Our conclusion that for unsuccessful shocks near threshold the earliest site represents a continuation of preceding VF is just the opposite of the conclusion drawn by Ideker's group (Chen et al. and Shibata et al.). They used an indirect analysis technique examining the time from the shock to the first postshock activation and concluded that unsuccessful shocks near threshold halt all activation fronts, after which VF regenerates. Their findings are based on the finding of an "isoelectric window" of variable duration after such an unsuccessful defibrillation attempt. They did not incorporate the inherent variability that is present in activation sequences from any given site and from one VF episode to the next, nor the timing of the first postshock activation from the last preshock activation into their analysis. This previous study concluded that such unsuccessful shocks near threshold halt all activation fronts after which fibrillation is regenerated anew, but that for lower energy unsuccessful shocks the underlying fibrillation was not affected and simply continued in regions of lowest shock voltage gradient. Indeed, their first postshock activation for a subthreshold unsuccessful defibrillation attempt (Figure 4C, approximately channel 19) conveys the same information as our Figure 10. There are several differences between their study and our study, including the use of polarizable electrodes, blanking intervals of approximately 15–20 msec longer than ours, use of bipolar recording electrodes that are waveform direction dependent, the use of AC-coupled rather than DC-coupled electrogram recording techniques, and switched rather than continuously connected amplifier arrays. However, none of these differences are sufficient to explain the different conclusions. The different conclusions are based on the definition used to classify what is a continuation of VF.

At near defibrillation threshold shock levels, the vast majority of the ventricular myocardium has been effectively defibrillated, and indeed all fibrillating
activity in those areas so affected cases. This is true whether the defibrillation is successful or unsuccessful, and the coordinated appearance of the first postshock activation in Figures 9 and 11 attest to this fact. The remainder of the heart in these cases appears to behave as a simple excitable syncytium, but its loading effect may play an important role in whether a single residual fibrillating site goes on to rekindle global fibrillation or whether it self-extinguishes. Recent studies have emphasized the importance of the interactions between the kinetics of depolarizing currents (presumably sodium current) and the passive anisotropic properties in regulating the safety factor of propagating impulses. The kinetics of the ionic channels are markedly influenced from site to site by electrical load differences dictated by the downstream membrane capacitance to be discharged due to anisotropic structural complexities. These previous elegant studies used paced in vitro preparations, but presumably similar arguments may apply to the conditions required to sustain initially localized VF in situ.

The finding of the type of defibrillation where all fibrillating activity cases is not a new finding. It was clearly described in 1974 by Mower et al and termed pattern 1; it was subsequently renamed type A recovery by Chen et al. Similarly, the type B successful defibrillation recovery that has been previously described corresponds to successful defibrillation with incomplete termination of all fibrillating activity. Our findings have described similar phenom-ena but provide a different insight into the underlying mechanisms responsible for these findings. The exact mechanism of ventricular fibrillation is unknown; however, the majority of evidence points to a reen-tract etiology for this disturbance. If there are multiple reentrant loops or vortexes that are continu-ously migrating in the myocardium during fibrillation, then a possible explanation for defibrillation is the temporary electrical snipping of segments of these loops by either activation of partially refractory tissue and subsequent loop termination or by prolongation of the repolarization phase of tissue found to be in phase 2 or 3. Such action potential prolongation by defibrillation level shocks has been observed in vitro by intracellular recordings, in myocardial cell aggregates by extrastimulus techniques, and in isolated rabbit hearts by voltage-sensitive dye techniques, with all of these studies performed during a paced regular rhythm. Similar recordings have not yet been reported, to our knowledge, in vivo during a defibrillation attempt. It is interesting to speculate that the organized low-level biphasic wave-form observed in Figure 8 immediately after the shock in the three earliest sites is the extracellular manifestation of repolarization homogenization resultant from the successful defibrillation shock. Confirmation of the etiology of this biphasic wave-form awaits simultaneous extracellular and intracel-lular recordings in vivo. If this is indeed a primary mechanism of defibrillation, it is purely speculative at this point as to which of the several known membrane currents involved in the regulation of the action potential plateau would be involved, including the L-type Ca current, the Na+ “window” or slowly inactivating current, and the K+ currents. Insight gained into the responsible ionic mechanism may translate into more efficient means of achieving the desired goal.

In summary, a technique was devised for measuring the epicardial voltage gradient field produced by a defibrillation shock that could be used for a similar application in a clinical setting. With this technique, the critical mass hypothesis for defibrillation was verified to be applicable to one type of successful defibrillation with the required amount of myocardium affected definitely less than 100%. For the second distinct form of effective defibrillation, the total extinction hypothesis appears correct. Finally, unsuccessful defibrillation is adequately explained by the failure to defibrillate at least one region of myocardium, and no additional vulnerability arguments need to be invoked to explain unsuccessful defibrillation.

Acknowledgments

The authors wish to thank Medtronic for their contribution of defibrillation patch electrodes and the 2394 External Cardioverter/Defibrillator, Ms. Shelly Schilbe for preparation of the manuscript, and Ms. Katherine Jones for her technical assistance with the experiments and the data analysis.

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**KEY WORDS** • unipolar electrograms • cardiac electrophysiology • automatic implantable cardioverter-defibrillator • ventricular fibrillation
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Circulation. 1990;82:244-260
doi: 10.1161/01.CIR.82.1.244

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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http://circ.ahajournals.org/content/82/1/244

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